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* * * * * * * * * * * Welcome to STN International * * * * * * * * * * *

| | | | |
|------|----|--------|--|
| NEWS | 1 | | Web Page for STN Seminar Schedule - N. America |
| NEWS | 2 | AUG 06 | CAS REGISTRY enhanced with new experimental property tags |
| NEWS | 3 | AUG 06 | FSTA enhanced with new thesaurus edition |
| NEWS | 4 | AUG 13 | CA/CAplus enhanced with additional kind codes for granted patents |
| NEWS | 5 | AUG 20 | CA/CAplus enhanced with CAS indexing in pre-1907 records |
| NEWS | 6 | AUG 27 | Full-text patent databases enhanced with predefined patent family display formats from INPADOCDB |
| NEWS | 7 | AUG 27 | USPATOLD now available on STN |
| NEWS | 8 | AUG 28 | CAS REGISTRY enhanced with additional experimental spectral property data |
| NEWS | 9 | SEP 07 | STN AnaVist, Version 2.0, now available with Derwent World Patents Index |
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| NEWS | 12 | SEP 17 | CA/CAplus enhanced with printed CA page images from 1967-1998 |
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| NEWS | 16 | OCT 19 | BEILSTEIN updated with new compounds |
| NEWS | 17 | NOV 15 | Derwent Indian patent publication number format enhanced |
| NEWS | 18 | NOV 19 | WPIX enhanced with XML display format |
| NEWS | 19 | NOV 30 | ICSD reloaded with enhancements |
| NEWS | 20 | DEC 04 | LINPADOCDB now available on STN |
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| NEWS | 22 | DEC 17 | USPATOLD added to additional database clusters |
| NEWS | 23 | DEC 17 | IMSDRUGCONF removed from database clusters and STN |
| NEWS | 24 | DEC 17 | DGENE now includes more than 10 million sequences |
| NEWS | 25 | DEC 17 | TOXCENTER enhanced with 2008 MeSH vocabulary in MEDLINE segment |
| NEWS | 26 | DEC 17 | MEDLINE and LMEDLINE updated with 2008 MeSH vocabulary |
| NEWS | 27 | DEC 17 | CA/CAplus enhanced with new custom IPC display formats |
| NEWS | 28 | DEC 17 | STN Viewer enhanced with full-text patent content from USPATOLD |
| NEWS | 29 | JAN 02 | STN pricing information for 2008 now available |
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| NEWS | 31 | JAN 28 | USPATFULL, USPAT2, and USPATOLD enhanced with new custom IPC display formats |
| NEWS | 32 | JAN 28 | MARPAT searching enhanced |
| NEWS | 33 | JAN 28 | USGENE now provides USPTO sequence data within 3 days of publication |
| NEWS | 34 | JAN 28 | TOXCENTER enhanced with reloaded MEDLINE segment |
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NEWS EXPRESS 19 SEPTEMBER 2007: CURRENT WINDOWS VERSION IS V8.2,

CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP),
AND CURRENT DISCOVER FILE IS DATED 19 SEPTEMBER 2007.

| | |
|------------|---|
| NEWS HOURS | STN Operating Hours Plus Help Desk Availability |
| NEWS LOGIN | Welcome Banner and News Items |
| NEWS IPC8 | For general information regarding STN implementation of IPC 8 |

Enter NEWS followed by the item number or name to see news on that specific topic.

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FILE 'REGISTRY' ENTERED AT 13:08:35 ON 04 FEB 2008
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STRUCTURE FILE UPDATES: 3 FEB 2008 HIGHEST RN 1001389-12-3
DICTIONARY FILE UPDATES: 3 FEB 2008 HIGHEST RN 1001389-12-3

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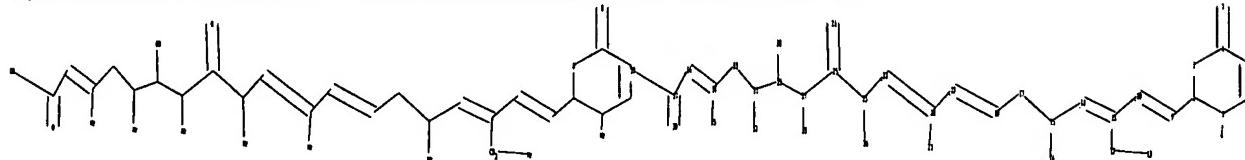
TSCA INFORMATION NOW CURRENT THROUGH June 29, 2007

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REGISTRY includes numerically searchable data for experimental and predicted properties as well as tags indicating availability of experimental property data in the original document. For information on property searching in REGISTRY, refer to:

<http://www.cas.org/support/stngen/stndoc/properties.html>

=>
Uploading C:\Program Files\Stnexp\Queries\10535672.str



chain nodes :

chain head
 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28
 29 30 31 32 33 34 35 36 37 38 39

```

ring nodes :
1 2 3 4 5 6
chain bonds :
1-8 2-9 4-7 9-10 10-11 11-12 11-14 12-13 14-15 15-16 15-17 17-18 18-19
19-20 20-21 20-22 22-23 23-24 23-25 25-26 25-27 27-28 27-29 29-30 29-31
31-32 31-33 33-34 34-35 34-36 36-37 37-38 37-39
ring bonds :
1-2 1-6 2-3 3-4 4-5 5-6
exact/norm bonds :
4-7 25-26 29-30
exact bonds :
1-2 1-6 1-8 2-3 2-9 3-4 4-5 5-6 9-10 10-11 11-12 11-14 12-13 14-15
15-16 15-17 17-18 18-19 19-20 20-21 20-22 22-23 23-24 23-25 25-27 27-28
27-29 29-31 31-32 31-33 33-34 34-35 34-36 36-37
normalized bonds :
37-38 37-39
isolated ring systems :
containing 1 :


```

```

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:CLASS 8:CLASS 9:CLASS 10:CLASS
11:CLASS 12:CLASS 13:CLASS 14:CLASS 15:CLASS 16:CLASS 17:CLASS 18:CLASS
19:CLASS 20:CLASS 21:CLASS 22:CLASS 23:CLASS 24:CLASS 25:CLASS 26:CLASS
27:CLASS 28:CLASS 29:CLASS 30:CLASS 31:CLASS 32:CLASS 33:CLASS 34:CLASS
35:CLASS 36:CLASS 37:CLASS 38:CLASS 39:CLASS


```

L1 STRUCTURE UPLOADED

```

=> d 11
L1 HAS NO ANSWERS
L1           STR

```

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

Structure attributes must be viewed using STN Express query preparation.

```

=> s 11
SAMPLE SEARCH INITIATED 13:09:01 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED -         4 TO ITERATE

```

| | | |
|------------------------|------------------------|-----------|
| 100.0% PROCESSED | 4 ITERATIONS | 0 ANSWERS |
| SEARCH TIME: 00.00.01 | | |
| FULL FILE PROJECTIONS: | ONLINE **COMPLETE** | |
| | BATCH **COMPLETE** | |
| PROJECTED ITERATIONS: | 4 TO 200 | |
| PROJECTED ANSWERS: | 0 TO 0 | |

L2 0 SEA SSS SAM L1

```

=> s 11 full
FULL SEARCH INITIATED 13:09:06 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED -         69 TO ITERATE

```

| | | |
|-----------------------|---------------|-----------|
| 100.0% PROCESSED | 69 ITERATIONS | 7 ANSWERS |
| SEARCH TIME: 00.00.01 | | |

L3 7 SEA SSS FUL L1

```

=> file caplus

```

| COST IN U.S. DOLLARS | SINCE FILE ENTRY | TOTAL SESSION |
|----------------------|------------------|---------------|
| FULL ESTIMATED COST | 178.36 | 179.20 |

FILE 'CAPLUS' ENTERED AT 13:09:26 ON 04 FEB 2008
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 FILE LAST UPDATED: 3 Feb 2008 (20080203/ED)

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=> s 13 full
 L4 144 L3

=> file reg
 COST IN U.S. DOLLARS SINCE FILE TOTAL
 ENTRY SESSION
 FULL ESTIMATED COST 0.48 179.68

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<http://www.cas.org/support/stngen/stndoc/properties.html>

=> s 13
 SAMPLE SEARCH INITIATED 13:09:51 FILE 'REGISTRY'
 SAMPLE SCREEN SEARCH COMPLETED - 4 TO ITERATE

100.0% PROCESSED 4 ITERATIONS 0 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE **COMPLETE**
 BATCH **COMPLETE**
PROJECTED ITERATIONS: 4 TO 200
PROJECTED ANSWERS: 0 TO 0

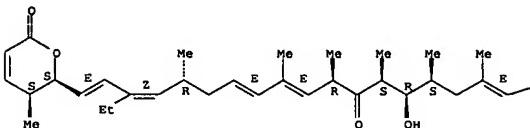
L5 0 SEA SSS SAM L1

=> d scan 13

L3 7 ANSWERS REGISTRY COPYRIGHT 2008 ACS on STN
IN 2,10,12,16,18-Nonadecapentaenoic acid,
19-[(2S,3S)-3,6-dihydro-3-methyl-6-
oxo-2H-pyran-2-yl]-17-ethyl-6-hydroxy-3,5,7,9,11,15-hexamethyl-8-oxo-,
monosodium salt, (2E,5S,6R,7S,9R,10E,12E,15R,16Z,18E)- (9CI)
MP C33 H48 O6 . Na

Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A



● Na

PAGE 1-B

—CO₂H

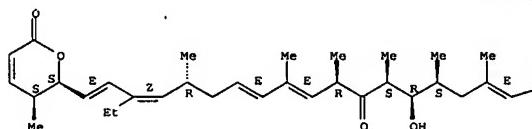
HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):1

L3 7 ANSWERS REGISTRY COPYRIGHT 2008 ACS on STN
IN 2,10,12,16,18-Nonadecapentaenoic acid, 19-(3,6-dihydro-3-methyl-6-oxo-2H-
pyran-2-yl)-17-ethyl-6-hydroxy-3,5,7,9,11,15-hexamethyl-8-oxo-, compd.
with N,N-diethylethanamine (1:1) (9CI)
MP C33 H48 O6 . C6 H15 N

CH 1

Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A



PAGE 1-B

—CO₂H

CH 2

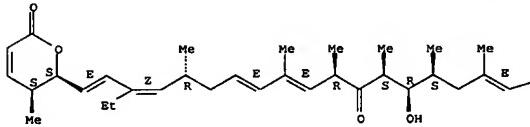


HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):1

L3 7 ANSWERS REGISTRY COPYRIGHT 2008 ACS on STN
IN 2,10,12,16,18-Nonadecapentaenoic acid,
19-[(2S,3S)-3,6-dihydro-3-methyl-6-
oxo-2H-pyran-2-yl]-17-ethyl-6-hydroxy-3,5,7,9,11,15-hexamethyl-8-oxo-,
(2E,5S,6R,7S,9R,10E,12E,15R,16Z,18E)-
MP C33 H48 O6
CI COM

Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A



PAGE 1-B

—CO₂H

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):0

=> file caplus
COST IN U.S. DOLLARS
FULL ESTIMATED COST

| SINCE FILE ENTRY | TOTAL SESSION |
|------------------|---------------|
| 3.68 | 183.36 |

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=> s 13 full
L6 144 L3

=> s 16 and leptomycin?
L7 647 LEPTOMYCIN?
136 L6 AND LEPTOMYCIN?

=> s 17 and metalloproteinas?
L8 29028 METALLOPROTEINAS?
2 L7 AND METALLOPROTEINAS?

=> s 17 and leptomycin B
L9 645 LEPTOMYCIN
11 LEPTOMYCINS
646 LEPTOMYCIN
(LEPTOMYCIN OR LEPTOMYCINS)
1750615 B
618 LEPTOMYCIN B
(LEPTOMYCIN(W) B)
136 L7 AND LEPTOMYCIN B

=> s 19 and py<2002
L10 21937595 PY<2002
55 L9 AND PY<2002

=> s 110 and skin
L11 272623 SKIN
10809 SKINS
278708 SKIN
(SKIN OR SKINS)
0 L10 AND SKIN

```
=> s l10 and fungal
      56895 FUNGAL
      15 FUNGALS
      56902 FUNGAL
          (FUNGAL OR FUNGALS)
L12      1 L10 AND FUNGAL

=> d ibib abs hitstr tot
```

DOCUMENT NUMBER: 128:215353

TITLE: Microbial conversion products of leptomycin

AUTHOR(S): Kuhnt, Michaela; Bitsch, Francis; Ponelle, Monique;

CORPORATE SOURCE: Sanglier, Jean-Jacques; Wang, Ying; Wolff, Barbara
 Core Technology Area, Research, Novartis Pharma Inc.,

SOURCE: Basel, CH-4002, Switz.
 Applied and Environmental Microbiology (1998)

CODEN: AEMIDP; ISSN: 0099-2240

PUBLISHER: American Society for Microbiology

DOCUMENT TYPE: JOURNAL

LANGUAGE: English

OTHER SOURCE(S): CASREACT 128:215353

AB Leptomycin B (LMB), a secondary metabolite produced by *Streptomyces* sp. strain ATS 1287 with known antifungal and antitumor effects, inhibits the nucleo-cytoplasmic translocation of the human immunodeficiency virus type 1 regulatory protein Rev and exhibits significant antiproliferative activity. Since LMB itself turned out to

be distinctly cytotoxic, a bioconversion screening with a selected set of 29 bacterial and 72 fungal strains was performed in order to obtain metabolites of LMB with reduced antiproliferative effects. Several derivs. of LMB, more polar than the parent compound and produced in yields

of >5%, were detected. Liquid chromatogr.-mass spectroscopy anal.

indicated the type of bioconversion. Fermen. (1 L scale) of those strains with high

rates of transformation were suitable for isolation and characterization of the most prominent metabolites. Thus, bioconversion of LMB with *Aspergillus flavus* ATCC 9170 and *Emericella unguis* ATCC 13431 served for isolation of the novel derivs. 26-hydroxy-LMB (30% was the concentration

of the metabolite [with respect to LMB] used for bioconversion) and LMB-24-glutaminamide (90%), resp. *Streptomyces rimosus* ATCC 28893 converted LMB into 4,11-dihydroxy-LMB (13%) and 2,3-dihydro-LMB (5%). Although the antiproliferative effects of the LMB metabolites could be reduced through microbial conversion, none of these metabolites inhibited the nuclear export of Rev better than LMB itself.

IT 87081-35-4, Leptomycin B

RL: BAC (Biological activity or effector, except adverse); BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence); (microbial leptomycin B metabolites as proliferation inhibitors)

RN 87081-35-4 CAPLUS

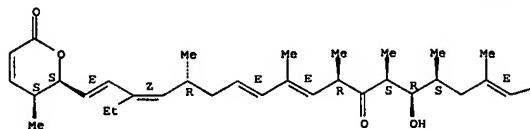
CN 2,10,12,16,18-Nonadecapentaenoic acid,

19-[(2S,3S)-3,6-dihydro-3-methyl-6-oxo-2H-pyran-2-yl]-17-ethyl-6-hydroxy-3,5,7,9,11,15-hexamethyl-8-oxo-, (2E,5S,6R,7S,9R,10E,12E,15R,16Z,18E)- (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.

PAGE 1-A



PAGE 1-B

-CO₂H

IT 204330-96-1, 4,11-Dihydroxyleptomycin B
 RL: BAC (Biological activity or effector, except adverse); BOC (Biological occurrence); BSU (Biological study, unclassified); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); OCCU (Occurrence); (microbial leptomycin B metabolites as proliferation inhibitors)

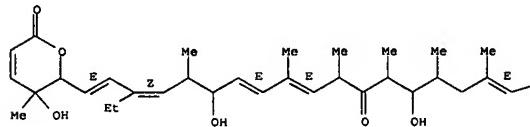
RN 204330-96-1 CAPLUS

CN 2,10,12,16,18-Nonadecapentaenoic acid,

19-[(3,6-dihydro-3-methyl-6-oxo-2H-pyran-2-yl)-17-ethyl-6-hydroxy-3,5,7,9,11,15-hexamethyl-8-oxo-, (9CI) (CA INDEX NAME)

Double bond geometry as shown.
 Currently available stereo shown.

PAGE 1-A



-CO₂H

REFERENCE COUNT: 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE REFORMAT

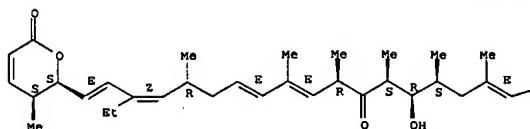
```
=> s l10 and tumor
    438664 TUMOR
    165222 TUMORS
    489727 TUMOR
          (TUMOR OR TUMORS)
L13      7 L10 AND TUMOR

=> d ibib abs hitstr tot
```

L13 ANSWER 1 OF 7 CAPLUS COPYRIGHT 2008 ACS on STN
 ACCESSION NUMBER: 2001:829425 CAPLUS
 DOCUMENT NUMBER: 136:80081
 TITLE: Dynamics of leptomycin B-sensitive nucleocytoplastic flux of parathyroid hormone-related protein
 AUTHOR(S): Lam, Mark H. C.; Henderson, Beric; Gillespie, Matthew T.; Jans, David A.
 CORPORATE SOURCE: Nuclear Signalling Laboratory, Division of Biochemistry and Molecular Biology, John Curtin School of Medical Research, Canberra, Australia
 SOURCE: Traffic (Copenhagen, Denmark) (2001), 2(11), 812-819
 PUBLISHER: Munksgaard International Publishers Ltd.
 DOCUMENT TYPE: JOURNAL
 LANGUAGE: English
 AB Parathyroid hormone-related protein is responsible for hypercalcemia induced by various tumors. The similarity of its N-terminus to that of parathyroid hormone enables parathyroid hormone-related protein to share parathyroid hormone's signaling properties, but the rest of the molecule possesses distinct functions including a role in the nucleus/nucleolus in reducing apoptosis and enhancing cell proliferation. We have previously shown that parathyroid hormone-related protein nuclear import is mediated by Importin β . Here we use fluorescence recovery after photobleaching for the first time to show that, in living cells, parathyroid hormone-related protein is exported from the nucleus in a leptomycin B-sensitive manner, implicating CRM1 as the parathyroid hormone-related protein nuclear export receptor. Leptomycin B treatment significantly reduced the rate of nuclear export 4–10-fold, thereby increasing parathyroid hormone-related protein concentration in the nucleus/nucleolus about 2-fold. Intriguingly, this also led to a 2-fold reduced nuclear import rate. Inhibiting the nuclear export of protein able to shuttle between nucleus and cytoplasm through distinct receptors thus can also affect nuclear import, indicating that the subcellular localization of a protein containing distinct nuclear import and export signals is the product of an integrated system. Although there have been several recent studies examining the dynamics of intranuclear transport using fluorescence recovery after photobleaching, this represents, to our knowledge, the first use of the technique to examine the kinetics of nucleocytoplastic flux in living cells.
 IT 87081-35-4, Leptomycin B
 RL: BSU (Biological study, unclassified); BIOL (Biological study) (parathyroid hormone-related protein leptomycin B -sensitive nucleocytoplastic flux and dynamics thereof)
 RN 87081-35-4 CAPLUS
 CN 2,10,12,16,18-Nonadecapentaenoic acid,
 19-((2S,3S)-3,6-dihydro-3-methyl-6-oxo-2H-pyran-2-yl)-17-ethyl-6-hydroxy-3,5,7,9,11,15-hexamethyl-8-oxo-, (2E,5S,6R,7S,9R,10E,12E,15R,16Z,18E)- (CA INDEX NAME)

Absolute stereochemistry.
 Double bond geometry as shown.

L13 ANSWER 1 OF 7 CAPLUS COPYRIGHT 2008 ACS on STN (Continued)
 PAGE 1-A



PAGE 1-B

REFERENCE COUNT: 40 THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE REFORMAT

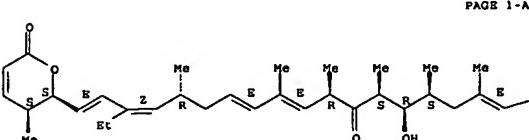
L13 ANSWER 2 OF 7 CAPLUS COPYRIGHT 2008 ACS on STN
 ACCESSION NUMBER: 2001:815253 CAPLUS
 DOCUMENT NUMBER: 136:49258
 TITLE: Suppressor of fused negatively regulates β -catenin signaling
 AUTHOR(S): Meng, Xianwang; Poon, Raymond; Zhang, Xiaoyun; Cheah, Alexander; Ding, Qi; Hui, Chi-Chung; Alman, Benjamin
 CORPORATE SOURCE: Program in Developmental Biology, The Hospital for Sick Children, University of Toronto, Toronto, ON, MSGIXB, Can.
 SOURCE: Journal of Biological Chemistry (2001), 276(43), 40113-40119
 PUBLISHER: American Society for Biochemistry and Molecular Biology
 DOCUMENT TYPE: JOURNAL
 LANGUAGE: English
 AB Suppressor of fused (Su(fu)) is a neg. regulator of the Hedgehog signaling pathway that controls the nuclear-cytoplasmic distribution of Gli/Ci transcription factors through direct protein-protein interactions. We show here that Su(fu) is present in a complex with the oncogenic transcriptional activator β -catenin and functions as a neg. regulator of Tcf-cell factor (Tcf)-dependent transcription. Overexpression of Su(fu) in SW480 (APCmut) colon cancer cells in which β -catenin protein is stabilized leads to a reduction in nuclear β -catenin levels and in Tcf-dependent transcription. This effect of Su(fu) overexpression can be blocked by treatment of these cells with leptomycin B, a specific inhibitor of CRM1-mediated nuclear export. Overexpression of Su(fu) suppresses growth of SW480 (APCmut) tumor cells in nude mice. These observations indicate that Su(fu) neg. regulates β -catenin signaling and that CRM-1-mediated nuclear export plays a role in this regulation. Our results also suggest that Su(fu) acts as a tumor suppressor.
 IT 87081-35-4, Leptomycin B
 RL: BSU (Biological study, unclassified); BIOL (Biological study) (suppressor of fused neg. regulates β -catenin signaling)
 RN 87081-35-4 CAPLUS
 CN 2,10,12,16,18-Nonadecapentaenoic acid,
 19-((2S,3S)-3,6-dihydro-3-methyl-6-oxo-2H-pyran-2-yl)-17-ethyl-6-hydroxy-3,5,7,9,11,15-hexamethyl-8-oxo-, (2E,5S,6R,7S,9R,10E,12E,15R,16Z,18E)- (CA INDEX NAME)

Absolute stereochemistry.
 Double bond geometry as shown.

L13 ANSWER 2 OF 7 CAPLUS COPYRIGHT 2008 ACS on STN (Continued)
 PAGE 1-B

REFERENCE COUNT: 39 THERE ARE 39 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE REFORMAT

CO2H
 CO2H

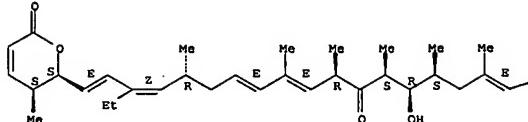


PAGE 1-A

L13 ANSWER 3 OF 7 CAPLUS COPYRIGHT 2008 ACS on STN
 ACCESSION NUMBER: 2000:780361 CAPLUS
 DOCUMENT NUMBER: 134:82300
 TITLE: Adenomatous polyposis coli protein contains two nuclear export signals and shuttles between the nucleus and cytoplasm.
 AUTHOR(S): Neufeld, Kristi L.; Nix, David A.; Bogerd, Hal; Kang, Yibin; Beckerle, Mary C.; Cullen, Bryan R.; White, Raymond L.
 CORPORATE SOURCE: Department of Oncological Sciences, Huntsman Cancer Institute, University of Utah, Salt Lake City, UT, 84112, USA
 SOURCE: Proceedings of the National Academy of Sciences of the United States of America (2000), 97(22), 12085-12090
 PUBLISHER: National Academy of Sciences
 DOCUMENT TYPE: JOURNAL
 LANGUAGE: English
 AB Mutational inactivation of the adenomatous polyposis coli (APC) tumor suppressor initiates most hereditary and sporadic colon carcinomas. Although APC protein is located in both the cytoplasm and the nucleus, the protein domains required to maintain a predominantly cytoplasmic localization are unknown. Here, we demonstrate that nuclear export of APC is mediated by two intrinsic, leucine-rich, nuclear export signals (NESs) located near the amino terminus. Each NES was able to induce the nuclear export of a fused carrier protein. Both APC NESs were independently able to interact with the Crm1 nuclear export factor and substitute for the HIV-1 Rev NES to mediate nuclear mRNA export. Both APC NESs functioned within the context of APC sequence: an amino-terminal APC peptide containing both NESs interacted with Crm1 and showed nuclear export in a heterokaryon nucleocytoplasmic shuttling assay. Also, mutation of both APC NESs resulted in the nuclear accumulation of the full-length, approx. 320-kDa APC protein, further establishing that the two intrinsic APC NESs are necessary for APC protein nuclear export. Moreover, endogenous APC accumulated in the nucleus of cells treated with the Crm1-specific nuclear export inhibitor leptomycin B. Together, these data indicate that APC is a nucleocytoplasmic shuttle protein whose predominantly cytoplasmic localization requires NES function and suggests that APC may be important for signaling between the nuclear and cytoplasmic compartments of epithelial cells.
 IT 87081-35-4, Leptomycin B
 RU: BAC (Biological activity or effector, except adverse); BSU
 (Biological study, unclassified); BIOL (Biological study)
 (nuclear export inhibitor leptomycin B blocks APC protein transport to cytoplasm)
 RN 87081-35-4 CAPLUS
 CN 2,10,12,16,18-Nonadecapentaenoic acid,
 19-((2S,3S)-3,6-dihydro-3-methyl-6-oxo-2H-pyran-2-yl)-17-ethyl-6-hydroxy-3,5,7,9,11,15-hexamethyl-8-oxo-, (2E,5S,6R,7S,9R,10E,12E,15R,16Z,18E)- (CA INDEX NAME)

Absolute stereochemistry.
 Double bond geometry as shown.

L13 ANSWER 3 OF 7 CAPLUS COPYRIGHT 2008 ACS on STN (Continued)
 PAGE 1-A



PAGE 1-B

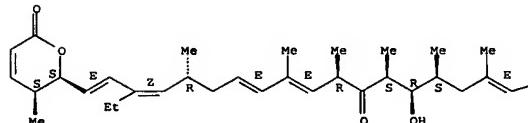
-CO₂H

REFERENCE COUNT: 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 4 OF 7 CAPLUS COPYRIGHT 2008 ACS on STN
 ACCESSION NUMBER: 2000:525399 CAPLUS
 DOCUMENT NUMBER: 133:217377
 TITLE: Activation of p53 in cervical carcinoma cells by small molecules
 AUTHOR(S): Hietanen, Sakari; Lain, Sonia; Krausz, Eberhard; Blattner, Christine; Lane, David P.
 CORPORATE SOURCE: CRC Cell Transformation Group, Department of Biochemistry, University of Dundee, Dundee, DD1 5EH, UK
 SOURCE: Proceedings of the National Academy of Sciences of the United States of America (2000), 97(15), 8501-8506
 PUBLISHER: National Academy of Sciences
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 AB In over 90% of cervical cancers and cancer-derived cell lines, the p53 tumor suppressor pathway is disrupted by human papillomavirus (HPV). The HPV E6 protein promotes the degradation of p53 and thus inhibits the stabilization and activation of p53 that would normally occur in response to HPV E7 oncogene expression. Restoration of p53 function in these cells by blocking this pathway should promote a selective therapeutic effect. Here we show that treatment with the small mol. nuclear export inhibitor, leptomycin B, and actinomycin D leads to the accumulation of transcriptionally active p53 in the nucleus of HeLa, CaSkI, and SiHa cells. Northern blot analyses showed that both actinomycin D and leptomycin B reduced the amount of HPV E6-E7 mRNA whereas combined treatment with the drugs showed almost complete disappearance of the viral mRNA. The combined treatment activated p53-dependent transcription, and increases in both p21WAF1/CIP1 and Hdm2 mRNA were seen. The combined treatment resulted in apoptotic death in the cells, as evidenced by nuclear fragmentation and PARP-cleavage indicative of caspase 3 activity. These effects were greatly reduced by expressing a dominant neg. p53 protein. The present study shows that small mols. can reactivate p53 in cervical carcinoma cells, and this reactivation is associated with an extensive bioresponse, including the induction of the apoptotic death of the cells.
 IT 87081-35-4, Leptomycin B
 RU: BAC (Biological activity or effector, except adverse); BSU
 (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (activation of p53 in cervical carcinoma cells by small mols.)
 RN 87081-35-4 CAPLUS
 CN 2,10,12,16,18-Nonadecapentaenoic acid,
 19-((2S,3S)-3,6-dihydro-3-methyl-6-oxo-2H-pyran-2-yl)-17-ethyl-6-hydroxy-3,5,7,9,11,15-hexamethyl-8-oxo-, (2E,5S,6R,7S,9R,10E,12E,15R,16Z,18E)- (CA INDEX NAME)

Absolute stereochemistry.
 Double bond geometry as shown.

L13 ANSWER 4 OF 7 CAPLUS COPYRIGHT 2008 ACS on STN (Continued)
 PAGE 1-A



PAGE 1-B

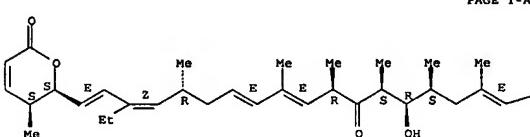
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REFERENCE COUNT: 54 THERE ARE 54 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 5 OF 7 CAPLUS COPYRIGHT 2008 ACS on STN
 ACCESSION NUMBER: 2000:9882 CAPLUS
 DOCUMENT NUMBER: 112:146316
 TITLE: Effects on normal fibroblasts and neuroblastoma cells of the activation of the p53 response by the nuclear export inhibitor leptomycin B
 AUTHOR(S): Smart, Philip; Lane, E. Birgitte; Lane, David P.; Midgley, Carol; Vojtesek, Bocek; Lain, Sonia
 CORPORATE SOURCE: CRC Cell Transformation Group, Department of Biochemistry, MSI/WTB, University of Dundee, Dundee, DDI, SEH, UK
 SOURCE: Oncogene (1999), 18(51), 7378-7386
 CODEN: ONCNE5; ISSN: 0950-9232
 PUBLISHER: Stockton Press
 DOCUMENT TYPE: Journal Article
 LANGUAGE: English
 AB P53 tumor suppressor protein levels and p53-dependent transcriptional activity have been recently shown to increase in cells treated with leptomycin B (LMB), an inhibitor of nuclear export. Expts. presented here show that LMB treatment leads to growth arrest and a senescence-like phenotype in human normal fibroblast cultures. This effect is reversible after removal of the drug and further passage by trypsinization. Instead, LMB has a strong cytotoxic effect on human neuroblastoma cell lines even at nanomolar concns. In both these cell types the effects of LMB are attenuated when the activity of the endogenous wild type p53 protein is abrogated by overexpression of a dominant neg. p53 mutant. We conclude that the induction of the p53 response by LMB plays an important role in the effects of this drug on cultured cells.

IT 87081-35-4, Leptomycin B
 RL: BAC (Biological activity or effector, except adverse); BSU
 (Biological study, unclassified); BIOL (Biological study)
 (effects of activation of the p53 response by leptomycin B on normal fibroblasts and neuroblastoma cells)
 RN 87081-35-4 CAPLUS
 CN 2,10,12,16,18-Nonadecapentaenoic acid,
 19-((2S,3S)-3,6-dihydro-3-methyl-6-oxo-2H-pyran-2-yl)-17-ethyl-6-hydroxy-3,5,7,9,11,15-hexamethyl-8-oxo-,
 (2E,5S,6R,7S,9R,10R,12E,15R,16Z,18E)- (CA INDEX NAME)

Absolute stereochemistry.
 Double bond geometry as shown.



PAGE 1-A

L13 ANSWER 6 OF 7 CAPLUS COPYRIGHT 2008 ACS on STN
 ACCESSION NUMBER: 1987:451496 CAPLUS
 DOCUMENT NUMBER: 107:51496
 TITLE: Studies on the new antibiotics kazusamycin and related substances

AUTHOR(S): Umezawa, Iwao; Komiyama, Kanki
 CORPORATE SOURCE: Kitasato Inst., Japan
 SOURCE: Gan to Kagaku Ryoho (1987), 14(3, Pt. 2), 658-64
 CODEN: GTKRDX; ISSN: 0385-0684

DOCUMENT TYPE: Journal Article
 LANGUAGE: Japanese
 AB Kazusamycins A and B and leptomycin B have a structure characteristic of an unsatd., branched-chain fatty acid with a terminal δ -lactone ring, and the former 2 agents show antimicrobial activity on some kinds of fungi. Kazusamycin A (KZM-A) showed cytotoxic activity on mammalian cells at very low concns. (nanogram per ml, range) in vitro. The antibiotic inhibited not only the growth of transplantable murine tumors and their metastases to the lung but also human mammary tumors inoculated into nude mice. KZM-A was rapidly distributed to the main organs of mice, and a percentage of the antibiotic was inactivated by binding to high-mol.-weight substances such as albumin. A large quantity of KZM-A was carried to the liver and excreted into the bile, but was then reabsorbed by the small intestine. The growth of tumor metastases (L5178Y cells) in the liver was suppressed by KZM-A. The antibiotic induced severe diarrhea by causing necrosis

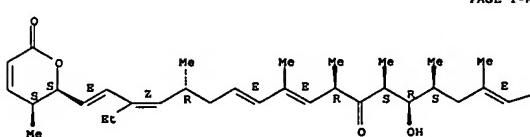
and/or lysis of the mucous membrane of the small intestine. In contrast to this, the degree of myelotoxicity was relatively slight. The active site of the

fatty acid of KZM-A appeared to consist of conjugated double bonds,

carboxylic acid, and hydroxyl moieties.

IT 87081-35-4, Leptomycin B
 RL: PRP (Properties)
 (antimicrobial and antitumor effects of)
 RN 87081-35-4 CAPLUS
 CN 2,10,12,16,18-Nonadecapentaenoic acid,
 19-((2S,3S)-3,6-dihydro-3-methyl-6-oxo-2H-pyran-2-yl)-17-ethyl-6-hydroxy-3,5,7,9,11,15-hexamethyl-8-oxo-,
 (2E,5S,6R,7S,9R,10R,12E,15R,16Z,18E)- (CA INDEX NAME)

Absolute stereochemistry.
 Double bond geometry as shown.



PAGE 1-A

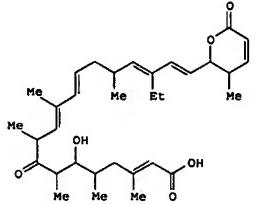
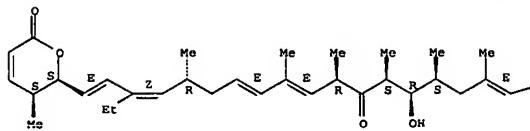
L13 ANSWER 5 OF 7 CAPLUS COPYRIGHT 2008 ACS on STN (Continued)

PAGE 1-B

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AB Leptomyycin B (I) [87081-35-4] increased the life span of mice bearing Erlich ascites tumors and Lewis lung carcinoma, but had only slight effects in mice bearing B-16 melanoma and P-388 lymphatic leukemia. I inhibited the growth of HeLa cells at a concentration of 4.9 ng/ml when the cells were exposed for 3 days. When

HeLa cells were exposed to I for 3 days, many polynuclear giant cells and masses of small nuclei appeared at a concentration of 1.25-2.5 ng/ml.

Thus, the antitumor activity of I appears to be due to a direct cytotoxic activity.

IT 87081-35-4

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES

(Uses) (neoplasm inhibition by, mechanism of)

RN 87081-35-4 CAPLUS

CN 2,10,12,16,18-Nonadecapentaenoic acid,

19-[(2S,3S)-3,6-dihydro-3-methyl-6-oxo-2H-pyran-2-yl]-17-ethyl-6-hydroxy-3,5,7,9,11,15-hexamethyl-8-oxo-, (2E,5S,6R,7S,9R,10E,12E,15R,16Z,18E)- (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

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FILE 'CAPLUS' ENTERED AT 13:09:26 ON 04 FEB 2008
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 L12 1 S L10 AND FUNGAL
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| CA SUBSCRIBER PRICE | ENTRY | SESSION |
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